

### **Remarks**

The Applicants will begin by addressing the rejections based on the prior art.

The Applicants note the rejection of Claims 1, 4-8, and 19 under 35 U.S.C. §102 over Iwai. The Applicants respectfully submit that the rejection is now moot with respect to Claim 19 in view of its cancellation. The Applicants also note the Examiner's helpful comment with respect to anticipation since the claims are not directed to a method of treating. All of Claims 1 and 4-8 have been amended to a method of treating. The Applicants therefore respectfully submit that Iwai is inapplicable. Withdrawal of the rejection is respectfully requested.

The Applicants note the rejection of Claims 1, 4-8, and 19 under 35 U.S.C. §102 over Brown. The Applicants respectfully submit that the rejection is now moot with respect to Claim 19 in view of its cancellation. The Applicants also note the Examiner's helpful comment with respect to anticipation since the claims are not directed to a method of treating. All of Claims 1 and 4-8 have been amended to a method of treating. The Applicants therefore respectfully submit that Brown is inapplicable. Withdrawal of the rejection is respectfully requested.

The Applicants note the rejection of Claims 1, 3-5 under 35 U.S.C. §102 over Simon. The Applicants also note the Examiner's helpful comment with respect to anticipation since the claims are not directed to a method of treating. All of Claims 1 and 3-5 have been amended to a method of treating. The Applicants therefore respectfully submit that Simon is inapplicable. Withdrawal of the rejection is respectfully requested.

The Applicants have amended the Specification to place it into more contemporary form. The Specification has also been amended in several locations such as on Pages 3, 8, 9, 12, and 13 to change "substituted" to "replaced." This will be discussed further below. Page 67 has also been

amended to correct a typographical error so that the page reference number now reads “998” instead of the erroneous “978.” Entry of the changes into the official file is respectfully requested.

The Applicants note the rejection of Claims 1-9 and 21-23 under 35 U.S.C. §112, first paragraph with respect to enablement. The Applicants first respectfully submit that the rejection is now moot with respect to Claims 9 and 21-23 in view of their cancellation. The Applicants nonetheless respectfully submit that Claims 1-8 are fully enabled for the reasons set forth in detail below.

The rejection takes the position that the Specification contains no prior art reference which can support “anticholinergic are used for treating urinary frequency or urinary incontinence.” The Applicants enclose for the Examiner’s convenience a copy of Cardozo et al. which demonstrates that anticholinergic drugs have been used for treating urinary frequency or urinary incontinence.

The rejection also takes the position that the Applicants’ disclosure contains no prior art reference which shows that rhythmic bladder contractions in female SD rats is a known animal model for urinary incontinence or urinary frequency. The Applicants enclose Dray et al. which demonstrates that such was, in fact, known to those skilled in the art.

The rejection further states that there is no teaching in the Applicants’ Specification or prior art regarding known utility of structurally closely related compounds for treating urinary incontinence or urinary frequency. In that regard, the Applicants note that they described morphine in their Specification on Page 2 at Lines 5-11 which was regarded as the most structurally closely related compound to the disclosed compounds which had a possibility for use for treating urinary incontinence or urinary frequency. The Applicants’ Specification specifically recites that:

Although it is known that morphine which is similar to the compounds of the present invention in the respect that it has morphinan structure although it does not contain a nitrogen-

containing heterocyclic group has an activity to inhibit micturition reflex (J. Pharm. Exp. Ther. 254(1984) etc.), it has strong side effects such as drug dependence, constipation and so on, so that it is not used as a therapeutic or prophylactic agent for urinary frequency or urinary incontinence.

Thus, the Applicants respectfully submit that there is a teaching that structurally related compounds have been employed for treating urinary incontinence or urinary frequency.

The rejection also takes the position that there is no teaching regarding any mechanism of action of the claimed compounds for the recited utility of treating or preventing urinary incontinence or urinary frequency. The Applicants respectfully submit that their original disclosure is replete with such disclosure. Specifically, the Applicants invite the Examiner's attention to Table 6 of the Specification. The Applicants disclose 87 compounds within the scope of Formula (I) that have been experimentally and factually confirmed. Therefore, the Applicants respectfully submit that they have directed those skilled in the art to a wide range of actual compounds that would easily, with almost no experimentation at all, be practiced.

It should also be noted based on the many, many compounds already tested by the Applicants that a large quantity of experimentation may not be "undue" experimentation. The fact that one skilled in the art may have to run a large number of experiments, which typically are quite repetitive, in no way implies that the experimentation is undue. This is particularly the case in the pharmaceutical area with respect to small molecule compounds where a large number of experiments are run on a very routine and surely not undue experimentation basis. The Applicants therefore respectfully submit that their original disclosure is fully enabling. Withdrawal of the rejection of Claims 1-9 is respectfully requested.

The Applicants note the rejection of Claims 1-9 and 11-23 under 35 U.S.C. §112, second paragraph. The Applicants have cancelled Claims 9, 19 and 21-23. The Applicants therefore respectfully submit that at least that portion of the rejection is now moot.

The Applicants have also amended various of the claims in accordance with the Examiner's helpful suggestion to remove the indefiniteness issues. Details are set forth below.

The rejection states in Claim 1 that there is no mention of replacing a carbon atom with sulfur, nitrogen or oxygen. As noted above, the Applicants have changed "substituted" to "replaced." In that regard, the word "substitute" should not be limited merely to replacement of a hydrogen atom. This is particularly true inasmuch as the original claim expressly stated that one or more of the carbon atoms therein may be substituted by nitrogen, oxygen or sulfur atoms. What this means is that the carbon may be replaced with nitrogen, oxygen or sulfur. In any event, for clarification purposes, the Applicants have changed "substituted" for "replaced."

The Applicants also note with appreciation the Examiner's helpful comments concerning the use of brackets. Appropriate changes have been made.

With respect to the terminology "therapeutic or prophylactic agent" language, the appropriate claims have been rewritten so that they no longer contain those terms.

With respect to Claim 9, that claim has been cancelled, thereby removing that portion of the rejection.

With respect to Claim 11 and the vagueness of the variables due to the lack of definition, the Applicants have made appropriate amendments to properly define the variables. Withdrawal of the rejection is respectfully requested.

The Applicants have made a number of other minor changes to various of the claims. For example, Claim 1 at Lines 16-17 has been amended to add "benzylidene, ethylidene,

cyclohexylmethyldene, butylidene, phenethylidene.” Support may be found in the Applicants’ Specification in Examples 21-2, 22-1, 23-1, 24-1, and 52, for example. Also, the changes to Line 27 of Claim 1 may be found on Page 3, Line 9 of the Applicants’ Specification. Finally, the change to Line 19 of Claim 1 is supported at the bottom of Page 5 of the Applicants’ Specification and extending through Page 8. Entry into the official file is respectfully requested.

The Applicants also enclose an Information Disclosure Statement including publication WO 95/03308, together with the usual Form PTO-1449. The Applicants respectfully request consideration on the merits and indication on Form PTO-1449 that such consideration has been given.

In light of the foregoing, the Applicants respectfully submit that the entire Application is now in condition for allowance, which is respectfully requested.

Respectfully submitted,



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